Endovascular Treatment of Brain Arteriovenous Malformations: the Toronto Experience

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Introduction

Brain arteriovenous malformations (BAVM) are errors of vascular morphogenesis. Although generally considered to be present at birth they are usually not apparent and become evident or symptomatic later in life.

Natural history data indicates that they have around 4% annual risk of hemorrhage and 1% risk of mortality with a combined rate of mortality and major morbidity of 2.7% per year. The Toronto AVM series had 3.4% annual risk of hemorrhage and on follow up only 45% of patients who bled made a complete recovery. Due to the relatively high lifetime risk of permanent neurological deficit or death from BAVM, treatment is indicated in most patients when location and angioarchitectural characteristics are favorable.

The endovascular treatment of BAVM has advanced rapidly during the last decades due to significant improvements in imaging and materials as well as well as embolic agents.

Parallel to this has been increased understanding of the pathophysiology and natural history. Endovascular treatment of BAVM started in Toronto in 1984.

The purpose of this review is to summarize the results of the University of Toronto Brain Vascular Malformation group and to compare treatment results and complications from the last two decades.

Methods

The University of Toronto Brain Vascular Malformation Group keeps a database on all BAVM patients evaluated and treated by the group. The data was collected retrospectively form 1984 to 1991 and from then prospectively. Currently 973 patients diagnosed with BAVM are registered in the database. All endovascular procedures were carried out at the Toronto Western Hospital and The Hospital for Sick Children. Patients with Vein of Galen malformations and cranial dural arteriovenous fistulas were excluded from this analysis. Two periods were analysed 1984-1993 and 1994-2004. Analyzed data includes demographic information, clinical presentation, initial neurological examination, technical aspects of the endovascular procedure, complications and outcomes. Complications related to embolization were defined as occurring within one month of the procedure. The severity of any complications was assessed with the Modified Rankin Scale (MRS). The purpose of the embolization was classified as an attempt to cure, pre-radiation, pre-operative or palliative treatment.

From 1984 to 1994 almost all embolization procedures were performed under neurolept anesthesia. Since 1995, general anesthesia has been routinely employed, and biplane digital subtraction angiography has been used since 1999. All patients are systemically anticoagulat-

Table 1 **Patient Characteristics and Clinical Presentation**

	1984-1993	1994-2004
	Number (%)	Number (%)
Total number of patients	184	155
Total number of embolizations	314	252
Male/Female	130/184	110/142
Presentation		
Symptomatic	Check (95)	145 (94)
Intracranial hemorrhage	72 (39%)	76 (49)
Headache	78 (42)	77 (50)
Seizure	91 (49)	61 (39)
Bruit	5 (3)	9 (6)
Neurological deficit	58 (32)	57 (37)
Motor	25 (14)	26 (17)
Sensory	6 (3%)	17 (11)
Visual	12 (7)	15 (10)
Cognitive	14 (8)	14 (9)
Cranial nerve	4 (2)	13 (8)
Speech	14 (8)	12 (8)

ed with heparin and Activated Clotting Time (ACT) kept between 250 and 350 seconds. Sheaths, guide catheters and microcatheters are continuously flushed using pressurized infusions. A calibrated leak balloon system and a propulsion chamber were used for intracranial catheterization until 1987. Since then, technical advances in microcatheters have allowed distal superselective catheterization. Both flow directed and over-the-wire catheter systems have been used. The goal has been the intra-nidal deposition of liquid embolic agent. More recently, for most preoperative embolizations, the goal has been arterial ligation without nidal deposition. Isobutyl-2-cyanoacrylate was the liquid embolic agent used until 1988. Thereafter, N-butyl cyanoacrylate was used. Dexamethasone is given (8 mg po/iv tid) for 2 days beginning at the time of the procedure. The patients are observed in a neuro-step-down unit overnight and then leave hospital on post-embolization day 2.

Results

From 1984-2004, 339 patients underwent 566 embolizations of a BAVM at the Toronto Western Hospital and Hospital for Sick Children in Toronto. The patient characteristics and presentation for the two periods are summarized in table 1. The majority of the patients were symptomatic with seizure being the most common form of presentation. In the first period 39% of the patients presented with intracranial hemorrhage and 49% in the second. The therapeutic strategy for BAVM embolization changed considerably. In the first period the majority of the embolizations were preformed

Table 2 **Therapeutic Strategy and Number of Vessels Embolized**

	1984-1993	1994-2004
	Number (%)	Number (%)
Total number of embolizations	314	252
Pre-operative embo	61 (19)	78 (31)
Pre-radiation embo	200 (64)	97 (38)
Curative embo	31(10)	41 (16)
Palliative embo	20 (6)	37 (15)
Unable to embo	48 (18)	42 (17)
Number of vessels embolized		
1	143 (54)	73 (35)
2	85 (32)	61 (29)
3	30 (11)	35 (17)
4	2 (1)	22 (10)
5	0	5 (2)
6	0	3 (1)
Unkown	6 (2)	0

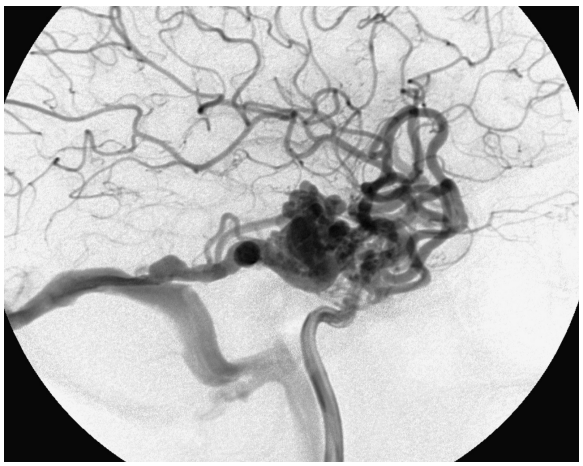
to shrink the AVM in preparation for radiosurgery (64%). In the second period the proportion of patients treated for this purpose had diminished to 38% with more patients having pre-operative, intentional curative or palliative embolization (62%). The number of patients where it was found to be unsafe or not possible to embolize was similar between the two periods. When the intention was to cure the BAVM with embolization alone the cure rate was 29% (missing data on cure rates in 4 patients) in the first period and 34.1% in the second period.

The mean number of vessels embolized per procedure increased from 1.3 (with 6 patients

Table 3 **Complications Related to Embolizations of BAVM**

	1984-1993	1994-2004
	Number (%)	Number (%)
Total number of embolizations	314	252
Complications	24 (7.6)	25 (9.9)
Clinically relevant	15 (4.8)	15 (5.9)
Transient neurological deficit	4 (1.3)	6 (2.4)
Permanent neurological deficit	6 (1.9)	7 (2.8)
Death	5 (1.6)	2 (0.79)

A



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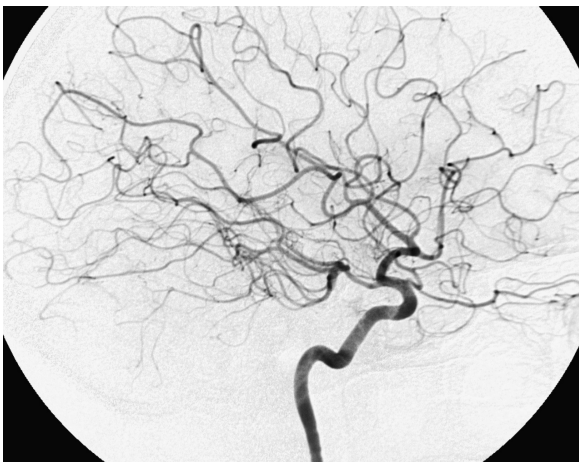
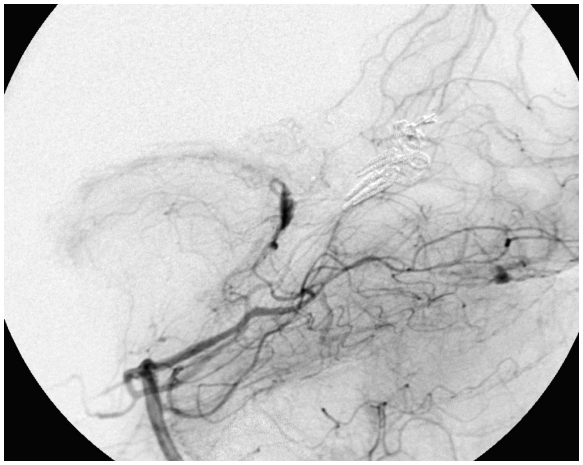


Figure 1 A) 46 year-old female with an incidentally discovered right temporal BAVM Spetzler-Martin Grade 2. Pre-embolization angiogram. B) 9 months follow up angiogram showing complete obliteration after a single session of transarterial glue embolization with nidal pentration.

A



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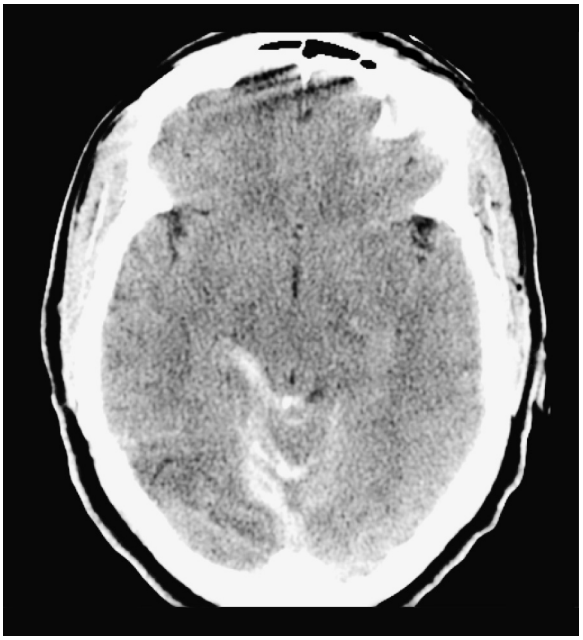

Figure 2 A) 30 year-old female diagnosed with a right occipital BAVM partially treated previously with glue embolization and surgery. After glue embolization, extravasation of contrast was observed. Heparinization was immediately reversed. B) Immediate head CT Scan showing local hemorrhage and contrast extravasation in the subarachnoid space. The patient was extubated and woke up neurologically intact.

excluded because of missing data in the first period) to 1.7 with 12% having 4 or more vessels being embolized vs. 1% in the first period (table 2.). If only patients who had embolization are analysed during the first period and the second period the mean number of vessels embolized per session were 1.5 vs. 2.1, respectively.

The rate of complications increased slightly in the second period from 7.6% to 9.9% with clinically significant complications rising from 4.8% to 5.9% (table 3). In the second period however, greater number of vessels were embolized, 431 v.s. 322 (data on six patients missing on number of vessels embolized in the first period). Transient or permanent neurological deficits were higher in the second period but death related to embolization decreased from 1.6% in the first period to 0.79% in the second period.

Discussion

The therapeutic strategy of AVM embolization has changed during the years of this study. In the second period a more aggressive approach was evident by more selective catheterization and greater number of glue injections per session. This is most likely a result of technical improvements in imaging and materials. Embolization of AVMs in eloquent locations can lead to ischemic injury of brain tissue adjacent to the nidus. Prior to the introduction of the newer variable stiffness microcatheters, many glue injections in our experience were performed from a pre-nidal position using free-flow technique. Small normal arteries supplying eloquent cortex may not have been visualized especially with the poorer angiographic images in the procedures performed under neurolept anesthesia. Now, using general anesthesia and, when possible, a wedged intranidal microcatheter position.

For nidus size <3 cm, single modality treatment is favored, whether it be surgery, radiosurgery, or embolization. Nidus size <3 cm with a single dominant arterial feeder have a high chance of cure with embolization. Additionally, if the diagnostic angiogram shows intranidal aneurysms or pseudoaneurysms, then embolization can be directed towards these weak-points prior to more definitive therapy. For nidus size >3 cm, in our experience, curative embolization has been rare. Instead, embolization has an adjunctive role in a multimodality treatment program. In this series the intention to cure increased between the two periods from 10%-16% (figure 1). The cure rate however remained similar with around 30% being cured with embolization alone in this group of patients.

With radiosurgery, embolization produces targeted size reduction. With surgery, embolization decreases blood flow through the nidus thereby making perinidal dissection less bloody and tedious. Less frequently, embolization can occlude deep feeders to an AVM nidus such as lenticulostriate perforator supply that would be encountered towards the end of nidus dissection. More recently, the goal of pre-operative embolization has been pure arterial ligation without nidal glue deposition to minimize the risk of venous glue placement.

Mortality and morbidity associated with endovascular treatment of BAVM in large clinical series is low[2-8]. Recent reports have shown mortality rates of 1.1-3.7% and morbidity of 3.8-14%. In this series the rate of complications with permanent neurological deficit increased from 1.9% to 2.8%. This is most likely related to the more aggressive approach discussed previously. This could be also a result of better documentation in the latter period with prospectively accumulated data. The mortality associated with endovascular treatment in this series is low compared to other published series. In the first period it was 1.6% and dropped to 0.79% in the second period with the last death occurring in 1994.

Hartman et al. reported on the risk of endovascular treatment of BAVMs in 233 patients. The mortality rate was 1% and 14% suffered new neurologic deficits. Of the latter, only 2% were persistent and disabling. They found that increasing patient age, absence of a pretreatment neurological deficit, and number of embolization sessions were associated with new post-embolization neurological deficits.

Taylor et al. reported the complications of BAVM preoperative embolization6. Two hundred and one patients underwent 339 embolization sessions using a variety of embolic agents including polyvinyl alcohol particles, N-butyl cyanoacrylate, detachable coils, and the liquid polymer Onyx. Mortality occurred in 2% and permanent neurologic deficit in 9% of patients. None of the demographic, anatomical, or procedural factors that they studied were associated with a poor outcome.

Glue deposition in nidal draining veins is a risk factor for embolization complications in our experience and also in the literature. We have found microcatheter injections under general anesthesia and high magnification extremely useful to clarify the transition from nidus to draining vein. This analysis allows us to predict where venous glue entry is likely to occur and to stop or pause the glue injection as necessary. The last post-embolization hemorrhage producing death or disabling morbidity was in 1995. The last microcatheter left intravascularly because of the catheter tip was attached to the glue cast was in 1997.

Conclusions

The overall rates of embolization related mortality and disabling morbidity in both periods are low. During the second period, there

has been an important, clinically relevant reduction in embolization complications producing death. We believe this is not only a reflection of improved angiographic equipment and microcatheters but, more importantly, is proof of the value of clinical judgement and experience. BAVMs should be managed in a multidisciplinary group that has special interest and commitment to patients with neurovascular diseases.

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